

REMARKS

Claims 91-93 and 95-97 were pending. Claims 92, 93, and 97 were cancelled. Claims 91, 95, and 96 were amended. Claims 140-149 were added. Therefore, claims 91, 95, 96, and 140-149 will be pending upon entry of the present amendment.

No new matter has been added. Support for the amendments to claim 91 can be found in the specification as originally filed, for example, at least at, page 35, lines 2-7 and 27-33. Claims 95 and 96 were amended to no longer depend from canceled independent claims. Support for new claim 140 can be found, for example, in the specification as originally filed, at least at page 17, lines 21-22, and page 26, lines 7-12. Support for claims 142-149 can be found, for example, in the specification as originally filed, for example, at least at page 35, lines 27-33.

Cancellation of and/or amendments to the claims should in no way be construed as an acquiescence to any of the Examiner's objections and/or rejections. The cancellation of and/or amendments to the claims are being made solely to expedite prosecution of the above-identified application. Applicants reserve the option to further prosecute the same or similar claims in the present or another patent application. The amendments made to the claims are not related to any issues of patentability.

Personal Interview with Examiner and Examiner's Supervisor

Applicants would like to thank Examiner Calamita and her supervisor, Examiner Fredman, for meeting with Applicants' attorneys on September 14, 2006. The claims as presented herein were discussed during the interview.

In particular, the Examiners suggested that the claims be amended to recite that the methods of the invention were for "identifying small molecules indicative of a disorder" and that "the small molecule profile is obtained using one or more techniques which detect 50% or more of the molecules in the sample." Applicants' attorney notes that the claims as presented herein have been amended according to the Examiners' suggestions.

Furthermore, it was agreed that a declaration presenting data for a plurality of disease states would be submitted. The Examiners indicated that presentation of sufficient data in declaration form would overcome the rejection of the claims under 35 U.S.C. § 112, first paragraph. Applicants' attorney notes that a declaration presenting data for six nervous system disorders is filed concurrently herewith.

Rejection of Claims 91 and 92 under Judicially Created Doctrine of Obviousness Type Double Patenting

Claims 91 and 92 are rejected on the grounds of obviousness type double patenting as being unpatentable over claim 1 of U.S. Patent No. 7,005,255. In particular, the Examiner is of the opinion that “[a]lthough the conflicting claims are not identical, they are not patentably distinct from each other because instant claims 91 and 92 are drawn to methods of correlating small molecules to disease states.” Claim 92 has been cancelled, thus rendering its rejection moot.

While in no way admitting that the present claims are obvious over claim 1 of U.S. Patent No. 7,005,255, Applicants respectfully submit herewith a terminal disclaimer in compliance with 37 C.F.R 1.321(b) and (c), which will obviate the rejection.

Provisional Rejections of Claims 91 and 92 under Judicially Created Doctrine of Obviousness Type Double Patenting

Claims 91 and 92 are rejected on the grounds of non-statutory obviousness type double patenting as being unpatentable over claim 1 of U.S.S.N. 11/301,077, claim 1 of U.S.S.N. 11/301,078, claim 1 of U.S.S.N. 11/301,079, claims 1-7 of U.S.S.N. 11/357,732, and claim 1 of U.S.S.N. 11/405,033. Claim 92 has been cancelled, thus rendering its provisional rejection moot.

With respect to claim 1 of U.S.S.N. 11/301,077, claim 1 of U.S.S.N. 11/301,078, claim 1 of U.S.S.N. 11/301,079, and claims 1-7 of U.S.S.N. 11/357,732, Applicants respectfully submit that, while in no way admitting that the present claims are obvious over the aforementioned claims, upon allowance of the present claims and the allowance of the aforementioned claims, Applicants will consider submitting a terminal disclaimer in compliance with 37 C.F.R 1.321(b) and (c) if appropriate, which will obviate the rejection.

With respect to U.S.S.N. 11/405,033, Applicants note that claim 1 of the ‘033 application is directed to a method for identifying small molecules affected by an agent. Applicants note that in the Restriction Requirement mailed from the United States Patent and Trademark Office on May 17, 2006, the Examiner found that metabolomically monitoring the response to a therapeutic agent was patentably distinct from methods for metabolomically facilitating the diagnosis of a disease state. Applicants submit that the instant claims are non-obvious in view of claim 1 of U.S.S.N. 11/405,033, and request that this provisional rejection of claim 91 be withdrawn.

Rejection of Claims 91-93 and 95-97 under 35 U.S.C. § 112, first paragraph

Claims 91-93 and 95-97 are rejected under 35 U.S.C. § 112, first paragraph, because “the specification does not provide enablement for determining the presence of or predisposition for any disease based on a small molecule profile. Applicants note that claims 92, 93, and 97 have been cancelled, thus rendering the rejection of those claims moot. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.” Applicants disagree.

Applicants note that in the personal interview with the Examiner and the Examiner’s supervisor a declaration presenting data which shows, for example, that the specification would have enabled an ordinarily skilled artisan at the time the application was filed to practice the invention was discussed. The Examiners agreed that such a declaration would help Applicants overcome the rejection of the claims under 35 U.S.C. § 112, first paragraph. Therefore, Applicants submit herewith a declaration of John Ryals, Ph.D. which presents data showing that the specification would have enabled an ordinarily skilled artisan at the time the application was filed to practice the invention.

Declaration

The attached declaration of John Ryals, Ph.D. shows how an ordinarily skilled artisan, at the time the application was filed, would have been able to use the methods described in the specification to identify small molecules indicative of particular nervous system disorders.

In particular, the declaration describes how small molecule profiles have been obtained and compared using the methods described in the originally filed specification to identify small molecules indicative of particular nervous system disorders.

In the declaration, it is described that samples of plasma were taken from both subjects with specific nervous system disorders and control subjects. The samples were then analyzed using techniques such as GC-MS and LC-MS and individual compounds were identified using techniques known in the art, such as NMR. These techniques were described in the specification, as originally filed, for example, at least at page 13, lines 12-16 and page 71, lines 6-11. Once obtained, the concentrations of particular small molecules for each disorder were graphed using computer programs. Computer analysis of the data was described in the specification, as originally filed, for example, at least at page 7, line 30 through page 8, line 4. The resulting data, presented in the declaration, show that by using the methods of the invention, compounds indicative of amyotrophic

lateral sclerosis, Alzheimer's disease, Huntington's disease, Parkinson's disease, depression, and schizophrenia have been found.

Accordingly, Applicants assert that the claimed invention is supported by the disclosure in the specification, in such a way as to enable one of ordinary skill in the art at the time the application was filed, to practice the invention. The ordinarily skilled artisan, in possession of the instant specification, would have been able to identify compounds indicative of a nervous system disorder by comparing a small molecule profile of a subject having the disorder to a standard small molecule profile, and thus been able to identify small molecules indicative of the nervous system disorder. Therefore, Applicants respectfully request that this rejection of claims 91, 95, and 96 under 35 U.S.C. § 112, first paragraph be withdrawn.

Rejection of Claims 91-93 and 95-97 under 35 U.S.C. § 102 (b)

Claims 91-93 and 95-97 are rejected under 35 U.S.C. § 102 (b) as being anticipated by Siman (U.S. Patent No. 5,871,712). Applicants note that claims 92, 93, and 97 have been cancelled, thus rendering the rejection of those claims moot.

The present invention is directed to identifying small molecules indicative of nervous system disorders, by comparing small molecule profiles which were obtained using one or more techniques which detect 50% or more of the small molecules in the sample.

The Siman reference describes a method for detecting calpain activation by detecting levels of calpain-generated spectrin BDP's using antibodies that specifically bind to these proteins. By design, Siman's antibodies only detect spectrin BDPs, and do not detect small molecule profiles. Accordingly, the reference fails to anticipate the claims. The reference only teaches detection of spectrin BDPs, not 50% or more of the small molecules in the sample as required by Applicants.

Therefore, Applicants respectfully submit that Siman does not teach or suggest the presently claimed invention and request that the rejection of claims 91, 95 and 96 under 35 U.S.C. § 102 (b) be withdrawn.

Rejection of Claims 91-93 and 95-97 under 35 U.S.C. § 102 (e)

Claims 91-93 and 95-97 are rejected under 35 U.S.C. § 102(e) as being anticipated by Niebroj-Dobosz *et al.* (*Acta Neurol. Scan.* 1999 100:6-11). Applicants note that claims 92, 93, and 97 have been cancelled, thus rendering the rejection of those claims moot.

Niebroj-Dobosz *et al.* is directed to confirming the hypothesis that amino acids act as transmitters in amyotrophic lateral sclerosis. Niebroj-Dobosz used HPLC to test for the presence of excitotoxic amino acids. In Niebroj-Dobosz *et al.*, the presence of four amino acids were studied: aspartate, glutamate, glycine, and GABA. The techniques used by Niebroj-Dobosz are specific to removing the amino acids of interest from the sample through pre-column derivitization with fluorescent agents and then passing the derivatized amino acids through an HPLC column. The techniques used by Niebroj-Dobosz *et al.* only detect the amino acids of interest to them, and not 50% or more of the small molecules in the sample as claimed by Applicants in claim 91.

Therefore, Applicants respectfully submit that Niebroj-Dobosz *et al.* does not teach or suggest the presently claimed invention and request that this rejection of claims 91, 95 and 96 under 35 U.S.C. § 102 (e) be withdrawn.

Rejection of Claim 93 under 35 U.S.C. § 102 (e)

Claim 93 is rejected under 35 U.S.C. § 102 (e) as being anticipated by Kaser *et al.* (U.S. Patent No. 6,168,933). Claim 93 has been cancelled, thus rendering its rejection moot.

SUMMARY

It is respectfully submitted that this application is in condition for allowance. If there are any remaining issues or the Examiner believes that a telephone conversation with Applicants' attorney would be helpful in expediting the prosecution of this application, the Examiner is invited to call the undersigned at (617) 227-7400.

Dated: December 12, 2006

Respectfully submitted,

By 
Cynthia M. Soroos
Registration No.: 53,623
LAHIVE & COCKFIELD, LLP
One Post Office Square
Boston, Massachusetts 02109
(617) 227-7400
(617) 742-4214 (Fax)
Attorney/Agent For Applicant